

## REMARKS

Claims 1-7 are previously cancelled. Claims 8-15 were previously presented. Claims 12-15 were amended to provide a proper antecedent basis for use of the term "flexible film."

One feature of the present invention is the use of a two-ply laminated backing structure comprising:

- (1) a polyethylene terephthalate film as a drug non-adsorptive layer having a thickness of 0.1 to 10 $\mu$ m, and
- (2) a flexible polymer film, a non-woven fabric, or a woven fabric having a thickness of 1 to 200  $\mu$ m.

In addition, the pressure-sensitive adhesive layer containing female hormone (i.e., active ingredient) is laminated on the drug non-adsorptive layer side of the backing of the present invention.

To prevent the active ingredient being adsorbed to the backing, the backing has to have the drug non-adsorptive layer, and the pressure-sensitive adhesive layer is laminated on the drug non-adsorptive layer side of the backing, away from the flexible film.

The inventors found out that polyethylene terephthalate film prevents the adsorption of the active ingredient from a pressure-sensitive adhesive layer contained thereof, and made a backing for an external patch using this polyethylene terephthalate film having a thickness of 0.1 to 10  $\mu$ m as a drug non-adsorptive layer, by laminating with flexible film having a thickness of 1 to 200 $\mu$ m.

## Claim Rejections – 35 USC § 103

*Claims 9-10, 12 were rejected under 35 U.S.C. 103(a) as being unpatentable over Kwiatek et al. (US Patent 4,573,996) in view of Kawaji et al. (US 6,177,098) in view of Akemi et al. (US 5,242,951).*

1. The Examiner pointed out that Kwiatek discloses a device for the administration of an active agent to the skin or mucosa (title). Kwiatek discloses numerous embodiments with the Figures. In particular, the backing layer (12) which can be a laminate of two or more films, such as polyethylene terephthalate/polyethylene or a

polyethylene/metallized polyethylene terephthalate/polyethylene laminate (column 7, lines 1-5).

2. The disclosure of Kwiatek relates to the reservoir type device for the administration of an active agent, without seeping out of the active agent from the device during use and storage.

The reservoir pocket of the device in the Kwiatek reference is to prevent the seeping out of the active agent from the reservoir pocket during use and storage, and therefore, the backing member of Kwiatek is an impermeable member such as a film or a composite of films.

In the Kwiatek patent, there is the following description:

--- "The composite can be metallized (e.g., aluminized) film or a laminate of two or more films or a combination thereof. For example, a laminate of polyethylene terephthalate and polyethylene (i.e., PE/PET) or a polyethylene/metallized polyethylene terephthalate/polyethylene (i.e., PE/metallized PET/PE) laminate can be employed. The preferred polymers include polyethylene (PE), polypropylene (PP), polyvinyl chloride (PV) and polyethylene terephthalate (PET)." ---

(Please refer to column 6, lines 66 to column 7, line 5.)

The laminate of polyethylene terephthalate and polyethylene is disclosed as the material of the backing member for the reservoir of Kwiatek; however, there is description of which polymer is allocated to the inner side of the reservoir, that, which polymer contacts the active agent.

Additionally, the active ingredient of Kwiatek does not present in the reservoir as an adhesive layer as taught and claimed in the present application. The active agent may be present either alone or in combination with other active agents and/or a pharmaceutically acceptable carrier.

Therefore the device of Kwiatek is clearly different for the percutaneous absorption of the active agent when compared to that described and claimed in the present application.

Accordingly, in the Kwiatek reference, there is no description or suggestion that the polyethylene terephthalate (PET) prevent the adsorption of the active ingredient from the adhesive layer into the flexible layer, as disclosed in the present application.

Moreover, there is nothing in the reference that indicates that polyethylene terephthalate functions as a drug non-adsorptive layer in the construction of the Kwiatek reference.

3. Furthermore, in Kwiatek, there is the following description:

--- “However, a primary purpose is to prevent seepage of the active agent through the outer surface layer of the device so, if the outer surface is coated on the surface in contact with the remainder of the device with the active agent impermeable adhesive layer, the impermeable adhesive layer, this impermeable adhesive layer will perform this purpose even if the outer surface layer is not totally impermeable to the active agent. Thus, it is not necessary in all instances that the outer surface layer be impermeable to the active agent, although in most instances it normally is. . . .” (Emphasis added.)

(Please refer to column 6, lines 31 to 41)

Thus, the prevention of seepage of the active agent from the reservoir can be attained by the combination of the backing member (outer surface layer) and the active agent impermeable adhesive layer. That is, the backing member does not perfectly prevent the seeping of the active ingredient, such as a female hormone as described in the present invention, from the reservoir of the device of Kwiatek. Therefore, the Kwiatek reference does not describe nor suggest the specific features of the claims in the application, namely, the laminate structure comprising a flexible film as an outer layer and a polyethylene terephthalate film as a drug non-adsorptive layer.

To conclude, even though the laminate of polyethylene terephthalate and polyethylene (PET/PE) is described in the Kwiatek reference as the backing material, the purpose of the laminate structure comprising a flexible film as an outer layer and polyethylene terephthalate film as a drug non-adsorptive layer of the present application is clearly different from that shown in the Kwiatek patent.

4. As concerns the Kawaji et al. reference, Kawaji relates to a plaster for percutaneous absorption which comprises a laminated backing comprising a polyester

film/non-woven fabric of vinylon having an elasticity rate of more than 5% and severance rate of more than 0.5 kg/10 mm in which said polyester film has a thickness of 1.5 - 6.0  $\mu$ m, and the unit weight of the vinylon non-woven cloth is 3-12 g/m<sup>2</sup>. Polyester film (polyethylene terephthalate film) is used in the reference to prevent the sublimation of active ingredient from the adhesive layer, and to achieve ODT (Occlusive Dressing Technique) effect, and flexibility of the plaster.

In contrast, in the present application, a polyethylene terephthalate film is acting as a drug non-adsorptive layer, and therefore, the purpose of the present invention is clearly different from the invention of Kawaji et al.

Further, the laminate structure of the external patch of Kawaji et al. is as follows:

(Polyester film, i.e., polyethylene terephthalate film/non-woven fabric of vinylon/adhesive layer)//skin surface.

On the contrary, the laminate structure of the external patch of the present invention is as follows:

(Flexible polymer film/drug non-adsorptive layer, i.e., polyethylene terephthalate film/adhesive layer)//skin surface. Therefore, the laminate structure of the present invention is clearly different from that of Kawaji et al. Please note the chart shown on page 14 of the May 7, 2011 response showing the difference in layer orientation between the application and both Akemi and Kawaji preparations.

5. The invention of Akemi et al. relates to an estrogen-containing gel preparation which is to be applied to the surface of the skin so as to continuously administered estrogen to the living body via the skin surface. This estrogen-containing gel preparation comprises a substrate having on one surface thereof a cross-linked gel layer formed by crosslinking a composition comprising the following ingredients (a) to (c), the weight ratio of the ingredient (b) to the ingredient (c) being from 1.0/0.25 to 1.0/2.0:

- (a) estrogen;
- (b) an acrylate polymer; and
- (c) a liquid ingredient compatible with the ingredient (b).

The substrate of Akemi et al. the materials which would never suffer from any decrease in the content of the liquid ingredient or the estrogen containing in the crosslinked gel layer caused by the migration toward another surface of the substrate followed by leakage are preferred (column 2, line 29 to 36). Examples include sole film of polyester, nylon, polyethylene and so on, as well as laminated film thereof.

To improve the adhesiveness between the substrate and the crosslinked gel layer by anchoring effect, substrate in the form of laminate films composed of a nonporous sheet comprising one or more materials and a porous film and to form a crosslinked gel layer on the surface of the porous sheet (column 2, line 41 to 49).

However, Akemi et al. does not describe or suggest the using of the polyethylene terephthalate film as drug non-adsorption layer, and laminated with flexible polymer film, and a non-woven or woven fabric to consist the backing layer of present invention, as well as the superior effect of the present invention.

6. As mentioned above, the backing structures of Kawaji et al. and Akemi et al., and those purposes are clearly different from the backing of the present invention having the laminate structure comprising a flexible film as an outer layer and polyethylene terephthalate film as a drug non-adsorptive layer. Please note the chart shown on page 14 of the May 7, 2011 response showing the difference in layer orientation between the application and both Akemi and Kawaji preparations.

Therefore, for the above reasons, Claims 9-10, 12 are not obvious over Kwiatek et al. (US Patent 4,573,996) in view of Kawaji et al. (US 6,177,098) in view of Akemi et al. (US 5,242,951).

*Claims 8 and 14 were also rejected under 35 U.S.C. 103(a) as being unpatentable over over Kwiatek et al. (US Patent 4,573,996) in view of Kawaji et al. and Akemi et al. and further in view of Radloff et al. (WO 2002/038134). US 2004/0091521 was used as the English equivalent translation of WO 2002/038134.*

1. The above discussion of the Kwiatek, Kawaji, and Akemi references apply to this rejection as well and the response to this rejection includes all of the previously presented remarks and arguments.

2. The additional reference, Radloff et al. describes an active substance patch comprising a laminate coated on its skin-facing side with an adhesive which comprises an active substance, the laminate having at least two plies. The side of the patch remote from the skin is a barrier layer which is impervious to the active substance, while its skin-facing side carries a backing layer, and these two layers can be separated from one another.

Therefore, the laminate structure of the present application has the reverse layering when compared to layering taught by the Radloff reference.

The laminate structure of the patch of Radloff et al. is as follows:

(Barrier layer/backing layer/adhesive layer containing active substance//skin surface.

In contrast, the laminate structure of the external patch of the present application is as follows:

(Flexible polymer film/drug non-adsorptive layer, i.e., polyethylene terephthalate film/adhesive layer containing active substance//skin surface.

Please note the chart shown on page 14 of the May 7, 2011 response showing the difference in layer orientation between the application and Akemi, Kawaji and Radloff preparations.

Therefore, for the above reasons, Claims 8 and 14 are not obvious over Kwiatek et al. (US Patent 4,573,996) in view of Kawaji et al. and Akemi et al. and further in view of Radloff et al. (WO 2002/038134).

*Claims 9, 11 and 13 were rejected under 35 U.S.C. 103(a) as being unpatentable over Xia et al. (US 5,693,335) in view of Kwiatek et al. (US Patent 4,573,996) and further in view of Muraoka et al. (US 5,876,745).*

1. The above discussion of the Kwiatek, reference applies to this rejection as well and the response to this rejection includes all of the previously presented remarks and arguments.

2. In the Xia et al. reference, a single layer, or film of polymer or laminate of one or more polymer layer and metal foil is used as a backing layer. Examples of polymer

include polyvinylchloride; polyvinylidene chloride; polyolefins such as polyurethane; and polyester such as polyethylene terephthalate.

However, a backing layer composed of a laminate structure comprising a polyethylene terephthalate film having a thickness of 0.1 to 10  $\mu\text{m}$  and a flexible polymer film, a non-woven fabric or a woven fabric having a thickness of 1 to 200  $\mu\text{m}$  of the present invention is not described or suggested in Xia et al. As discussed on page 12 of the May 7, 2011 response, the Xia preparation is another example where the layer impermeable to the drug is on the outside, farthest layer from the skin, in the reverse orientation from that taught by applicants.

3. The laminate structure shown in the Muraoka et al reference comprises a porous and non-porous sheet. As discussed on page 13 of the previously response submitted on May 7, 2011, the nonporous layer 1 is on the outside, away from and not adjacent to the adhesive layer, in the opposite orientation as disclosed and claimed by applicants. Please note the chart shown on page 14 of the May 7, 2011 response showing the difference in layer orientation between the application and Muraoka. Xia was not included in this chart, but the “impermeable layer” of Xia is again the outermost layer.

Therefore, for the above reasons, Claims 9, 11 and 13 are not obvious over Xia et al. (US 5,693,335) in view of Kwiatek et al. (US Patent 4,573,996) and further in view of Muraoka et al. (US 5,876,745).

*Claim 8 and 15 were rejected under 35 U.S.C. 103(a) as being unpatentable over Xia et al. (US 5,693,335) in view of Kwiatek et al. (US Patent 4,573,996) and Muraoka et al. (US 5,876,745) and further in view of Radloff et al. (WO 2002/038134)*

The above discussion of the Kwiatek, Xia, Muraoka and Radloff references apply to this rejection as well and the response to this rejection includes all of the previously presented remarks and arguments.

Please note the chart shown on page 14 of the May 7, 2011 response showing the difference in layer orientation between the application and both Akemi and Kawaji preparations.

Therefore, for the above reasons, Claims 8 and 15 are not obvious over Xia et al. (US 5,693,335) in view of Kwiatek et al. (US Patent 4,573,996) and Muraoka et al. (US 5,876,745) and further in view of Radloff et al. (WO 2002/038134).

Additional differences between the applicants' disclosure and the references were discussed in depth in the May 7, 2010 response, which is incorporated in this response and not repeated for the sake of streamlining the prosecution.

### **Structural Elements**

The Kawaji, Akemi, Radloff, Xia and Akemi all place the barrier, impermeable, non-adsorptive layer on the outside of the preparation. The applicants teach a non-woven layer on the outside, with the barrier, impermeable, non-adsorptive layer in the middle, between the non-woven layer and adhesive layer containing the active ingredient. This layer is not on the outside. This difference structure is unobvious in light of the references which clearly place the barrier layer as the outermost layer.

## CONCLUSION

If the Examiner has any questions or suggested Examiner's amendments, the Examiner is respectfully requested to call the undersigned.

The Commissioner is hereby authorized to charge any additional fees, or to credit any overpayment, to Deposit Account No. 50-3195.

Respectfully submitted,

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